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SYNTHESIS OF PRECURSORS FOR BIOLOGICALLY ACTIVE LACTONES IV.

Rigorous Thesis

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A high width of biological activity of natural or synthetic unsaturated five membered lactones from the family of furan-2(5*H*)-ones, is the main reason why to synthesize new substances of this structure. The introductory part of the thesis deals with antineoplastic natural compounds of this type. Except of antitumour activity some unsaturated five membered lactones exhibit antifungal, antiviral, antibacterial effects, or inhibit the synthesis of cholesterol, for example.

The experimental project is an extension of my diploma thesis concerned with the synthesis of precursors for lactones. These precursors – methyl (*E*)- and (*Z*)-2-bromo-5-(subst.)arylpent-2-en-4-ynoates – were prepared by Sonogashira couplings. The parent substances for couplings were arylethynes (1-ethynyl-4-(methoxymethoxy)benzen, 1-ethynyl-2-nitrobenzene, 3-ethynylaniline, 2-ethynylpyridine) and methylesters of dihalogenated prop-2-enoic acid. The dominant products of the couplings were β-monoalkynylated esters, apart from them side products of homocouplings were obtained.

Reactions of *E*-methylesters of dihalogenated prop-2-enoic acid afford higher or comparable yields than the corresponding *Z*-methylesters of dihalogenated prop-2-enoic acid. *E*-isomers are stericly more suitable for couplings.

Only methyl (*E*)-2-bromo-5-(subst.)arylpent-2-en-4-ynoates are suitable for synthesis of potentially biologically active lactones because of steric reasons (these substances will be first hydrolyzed to acids, and the acids will be used for lactonization to 2-bromo-5-(subst.)arylmethylidenefuran-2(5*H*)-ones). The products of reactions with *Z*-isomers can serve as precursors for various other coumpounds.

The target compounds containing γ-butyrolactone moiety will be evaluated for their antineoplastic and antiviral activity.